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Are late-night eating habits and sleep duration associated with glycemic control in adult type 1 diabetes patients treated with insulin pumps?

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ABSTRACT

Aims/Introduction: Little is known about the impact of sleep duration and late-night snacking on glycemic control in patients with type 1 diabetes using insulin pumps. The aim of the present study was to examine whether late-night eating habits and short sleep duration are associated with glycemic control in continuous subcutaneous insulin infusion-treated type 1 diabetic patients.

Materials and Methods: We included 148 consecutive adult type 1 diabetic subjects using an insulin pump (100 women and 48 men). Participants completed a questionnaire regarding sleep duration (classified as short if ≤6 h) and late-night snacking. Other sources of information included medical records and data from blood glucose meters. Glycemic control was assessed by glycated hemoglobin (HbA1c) levels and mean self-monitoring of blood glucose (SMBG) readings.

Results: The mean age of patients was 26 years, mean type 1 diabetes duration was 13.4 years and mean HbA1c level was 7.2%. In a univariate regression analysis, sleep duration was a predictor of both HbA1c ($\beta = 0.51$, $P = 0.01$) and SMBG levels ($\beta = 11.4$, $P = 0.02$). Additionally, an association was found between frequent late-night snacking and higher SMBG readings (often snacking $\beta = 18.1$, $P = 0.05$), but not with increased HbA1c levels. In the multivariate linear regression, independent predictors for HbA1c and SMBG were sleep duration and patient age. In a univariate logistic regression, sleep duration and frequency of late-night snacking were not predictors of whether HbA1c target levels were achieved.

Conclusions: Short sleep duration, but not late-night snacking, seems to be associated with poorer glycemic control in type 1 diabetic patients treated with continuous subcutaneous insulin infusion.

INTRODUCTION

The Diabetes Control and Complications Trial (DCCT) proved that in type 1 diabetes, intensive insulin therapy as compared with conventional treatment improves long-term health outcomes[1]. The intensive insulin therapy can be implemented either with continuous subcutaneous insulin infusion (CSII) by a personal pump or multiple daily injections (MDI). The use of pump therapy has potential benefits for type 1 diabetic patients, because it offers a customized, flexible basal and bolus dosing to meet a patient's individual insulin requirement. This system of insulin delivery is not only associated with an improvement in glycemic control, but also increased physical and psychological well-being[2–6]. The enhanced lifestyle flexibility, mainly related to sleep and mealtimes, is one of the major reasons for choosing CSII for a growing number of type 1 diabetic patients[7,8]. However, concerns have also been raised whether greater dietary freedom associated with CSII could give a rise

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to undesirable behaviors; for example, related to food consumption[9]. One of them is late-night eating habits that might potentially impair glycemic control. Eating late can be also associated with shorter sleep duration[10]. Sleep is a physiological state that constitutes the most effective form of rest. However, over the past 100 years, the average sleep duration has shortened by 1.5 h/night[11]. Currently, in the USA, one in three adults sleeps less than 6.5 h/night[11,12]. A meta-analysis carried out on the general population found that short sleep duration and very long sleep duration were associated with an increased risk of cardiovascular disease, stroke and associated mortality[13]. Recent studies have shown that might may be a U-shaped relationship between sleep duration and glycemic control in type 2 diabetes[14,15]. It was also reported that patients with type 1 diabetes, as well as their families, slept for an insufficient number of hours, according to the recommendations[10].

The current study aimed to examine whether late eating habits and short sleep duration are associated with glycemic control, as assessed by glycated hemoglobin (HbA1c) levels and mean self-monitoring of blood glucose (SMBG) readings in CSII-treated adult type 1 diabetic patients.

MATERIALS AND METHODS

The present study was carried out at the Department of Metabolic Diseases, Krakow, a university referral center for diabetes care in southeastern Poland. The study population included 148 consecutive adult type 1 diabetic patients using insulin pumps (100 women and 48 men) who registered in 2013 and completed a questionnaire regarding topics such as subjective average sleep duration (classified as short sleep duration when ≤6 h and long sleep duration >6 h) and late night snacking habits (eating after 22.00 h rarely, sometimes or often). All invited type 1 diabetic patients completed the questionnaire; however, two participants did not provide any information about sleep duration. Type 1 diabetic patients less than 18 years-of-age and pregnant women were excluded from the present study. Other sources of information about patient characteristics (together with diabetic complications) included available medical records, as well as the results of biochemical tests (HbA1c measured using the high performance liquid chromatography method) and data from blood glucose meters, which were downloaded regularly onto a computer. Glycemic control was assessed by two parameters: HbA1c levels and mean SMBG readings calculated from glucose meter data. Information was also collected on subjective hypoglycemia perception defined as the level of glucose at which the subject perceives early symptoms of hypoglycemia. A hypoglycemic episode was defined as an event where glucose concentration measured with a glucose meter was 55 mg/dL or less, as defined by the Polish Diabetes Association during the time when the study was carried out[16].

Tests for differences between the two groups (Student's *t*-test or Mann–Whitney *U*-test), uni- and multivariate linear regression analyses, as well as uni- and multivariate logistic regression for predictors of reaching the therapeutic targets of HbA1c <7.0% (53 mmol/mol, as recommended by the American Diabetes Association) and HbA1c <6.5% (48 mmol/mol, as suggested by the Polish Diabetes Association) were used[16]. In the present multivariate analysis, the following characteristics were included as independent variables: sleep duration (long sleep duration as a baseline), frequency of late night snacking (dummy variable with rare snacking after 22.00 h as a baseline), body mass index, age and sex. *P*-values <0.05 were considered significant. The χ^2-test or Fisher's exact test were used for categorical variables. Statistical analysis was carried out using Statistica PL version 10.0 (StatSoft Inc, Tulsa, OK, USA) and R version 3.1.1 (http://www.r-project.org/).

The study protocol was approved by the ethical committee of the Jagiellonian University Medical College. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2008.

Informed consent was obtained from all patients included in the study.

RESULTS

Clinical characteristics of the patients are summarized in Table 1. The patients' mean age was 26.3 ± 9.0 years, mean type 1 diabetes duration was 13.4 ± 7.4 years, mean HbA1c level was 7.2 ± 1.0%, mean body mass index was 23.3 ± 3.1 kg/m^2, while mean night-time sleep duration was 7.2 ± 1.1 h. Most participants were free from chronic diabetic complications, as the proportion of patients with retinopathy, neuropathy and nephropathy were 7.43% (n = 11), 7.43% (n = 11) and 2.70% (n = 4), respectively. Short sleep duration (26.3% of patients) as compared with long sleep duration was associated with poorer glycemic control: HbA1c 7.6 vs 7.1%, P = 0.03; mean SMBG readings 159 vs 149 mg/dL, P = 0.05, respectively. Patients who slept longer tended to have more hypoglycemic episodes per 100 glucometer measurements (P = 0.05). It was also investigated whether there was a U-shaped relationship between sleep duration and glycemic control (with higher HbA1c levels in patients with an average self-reported sleep duration ≤6 h/night and ≥8 h/night compared with those with 6–8 h/night); however, there was no significant difference between the groups (P = 0.32). There was no association between sleep duration and late night snacking behavior (P = 0.33). Eating late, but not shorter sleep duration, was more frequently found in males treated with CSII (P = 0.01, P = 0.49, respectively). Patient characteristics, according to sleep duration are shown in Table 1.

When undertaking a univariate linear regression, sleep duration was found to be a predictor of both HbA1c (β = 0.51; P = 0.01) and SMBG levels (β = 11.4; P = 0.02). Additionally, it was found that the variable frequency of late night snacking (dummy variable with rare snacking after 22.00 h as a baseline)

Table 1 | Study group characteristics

Variable	Whole study group *n* (%)	Sleep ≤6 h *n* (%)	Sleep >6 h *n* (%)	*P*-value†
Sex (male/female)	48/100 (32.4/67.6)	14/25 (35.9/64.1)	32/75 (29.9/70.1)	0.4905
Retinopathy‡	11 (7.4)	4 (10.2)	7 (6.5)	0.4849
Neuropathy§	11 (7.4)	1 (2.6)	10 (9.3)	0.2889
Nephropathy¶	4 (2.7)	2 (5.1)	2 (1.9)	0.2897
Frequency of late-night snacking (rarely/sometimes/often)	80/57/11 (54.1/38.5/7.4)	18/19/2 (46.1/48.7/5.1)	61/38/8 (57/35.5/7.5)	0.3449
Patients with HbA1c <7%	61 (44.8)	13 (36.1)	47 (47.9)	0.2215
Patients with HbA1c <6.5%	36 (26.5)	8 (22.2)	28 (28.6)	0.4624

Variable	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	*P*-value†
HbA1c (%)	7.2	1.0	7.1	7.6	1.3	7.4	7.1	0.8	7.0	0.0293
Age at the examination (years)	26.3	9.0	23.0	26.8	9.1	24.0	26.3	9.0	23.0	0.6320
T1DM diagnosis age (years)	13.0	7.6	11.2	13.3	8.5	11.5	12.9	7.4	12.0	0.8490
Diabetes duration (years)	13.4	7.4	13.0	13.5	7.1	14.0	13.5	7.5	13.0	0.7265
Time on CSII (years)	4.8	3.5	4.5	5.0	3.3	5.5	4.8	3.6	4.5	0.5035
BMI (kg/m^2)	23.3	3.1	23.0	23.0	2.9	22.1	23.4	3.1	23.2	0.2519
Glycemia from glucose meter (mg/dL)	148.4	27.4	146.7	156.3	32.2	153.1	144.8	24.2	143.3	0.0491
No. blood glucose measurements per day (*n*)	6.4	3.0	5.7	6.5	2.8	6.2	6.4	3.1	5.7	0.7362
Daily insulin dose (IU)	46.6	14.1	44.5	45.8	13.6	43.6	46.8	14.3	44.8	0.7130
Daily insulin dose per kg of body mass (IU/kg)	0.69	0.16	0.70	0.68	0.19	0.68	0.69	0.15	0.70	0.9072
No. hypoglycemic episodes per 100 blood glucose measure (*n*)	5.3	5.4	4.0	5.1	7.6	2.6	5.4	4.4	4.3	0.0506
Sleep duration (h)	7.2	1.1	7.0	5.8	0.4	6.0	7.7	0.7	8.0	0.0000

BMI, body mass index, CSII, continuous subcutaneous insulin infusion; HbA1c, glycated hemoglobin; SD, standard deviation; T1DM, type 1 diabetes mellitus. †*P*-value for the comparison between short sleep duration group vs long sleep duration group is shown. ‡Retinopathy was diagnosed based on ophthalmological examination. §Neuropathy was defined as the presence of its clinical signs or symptoms during physical examination. ¶Nephropathy was diagnosed based on urinary albumin excretion above 30 mg/day or glomerular filtration rate <60 mL/min/1.73 m^2.

was a predictor of SMBG (often snacking $\beta = 18.1$; $P = 0.05$), but not of HbA1c levels ($P > 0.09$). In the multivariate linear regression analysis, independent predictors for HbA1c were the patient's age ($\beta = -0.02$, $P = 0.01$) and sleep duration ($\beta = 0.51$, $P = 0.01$). The analyzed model was significant ($P = 0.01$). In the multivariate regression analysis for mean SMBG readings, the same variables remained significant (patient's age [$\beta = -0.67$, $P = 0.01$] and sleep duration [$\beta = 11.5$, $P = 0.02$]).

In the univariate logistic regression analysis, sleep duration and frequency of late-night snacking were not predictors of achieving HbA1c expressed therapeutic targets (<6.5% [48 mmol/mol] or 7.0% [53 mmol/mol], respectively). In the multivariate logistic regression analysis that included age, body mass index and sex as independent variables, age was the only independent predictor of both therapeutic goals (OR 1.04, 95% confidence interval 1.00–1.09, for both analyses).

DISCUSSION

The present retrospective study is the first to assess a potential association between sleep duration and late-night snacking with glycemic control in type 1 diabetic patients treated with CSII. The mean night-time sleep duration for our cohort was 7.2 h, which is comparable with previous data from type 1 diabetic patients[17]. The key finding of the present study was that shorter sleep duration was associated with worse glycemic control after adjustment for potential confounders. One can attribute this finding to the fact that a shorter sleep duration produces insulin resistance through the increased secretion of stress and other hormones, such as ghrelin and leptin, which leads to neurohormonal dysregulation[10,18–21]. There has only been one previous study (cross-sectional) that showed a deteriorating effect of chronic sleep deprivation on glycemic control in patients with type 1 diabetes[10]. Interestingly, it was also reported that type 1 diabetic patients with a long history of the disease have poor subjective sleep quality, but no association between individual sleep characteristics and glycemic control was found[17]. There have also been some studies in healthy subjects proving that partial sleep restriction decreased glucose tolerance and induced insulin resistance[22,23]. Interestingly, the percentage of patients treated with CSII showing a potentially "unhealthy" habit of eating late was relatively high in the present study, although, late-night snacking was not an independent factor influencing glycemic control. It should be also

noted that both examined behaviors were not predictors of reaching glycemic goals, as defined by the HbA1c levels, although this could be at least partially attributed to the low power of the analysis.

The present report also had several additional limitations. It was a retrospective study; therefore, causality could not be identified, and the cumulative effect of temporal change in sleep duration could not be evaluated. Sleep duration was self-reported, thus, recall error might exist. The impact of potential confounders should also be mentioned. For example, we did not collect information about the nature of the patients' employment or the presence of possible concomitant conditions, such as obstructive sleep apnea. Thus, we cannot entirely exclude the contribution of these or other confounding factors to the study results. Additionally, the choice of cut-off points should perhaps be discussed. We have chosen 6 h to differentiate between short and long sleep duration based on previously published papers[14,15]. We have tried to stay consistent with these earlier reports. We also arbitrarily set the threshold for late eating to 22.00 h, as this complies with our common clinical practice in which we actively discourage patients to consume food after this time (unless justified by low glucose value). Finally, we have to acknowledge that the questionnaire used in the present research was not validated.

To conclude, we have found that shorter sleep duration, but not late-night snacking, was associated with poorer glycemic control in adult type 1 diabetic patients treated with CSII. It is advised in clinical practice that patients follow the recommended rules of sleep hygiene. Further research is required, especially in the assessment of the efficacy of lifestyle interventions on the course of type 1 diabetes.

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The authors declare no conflict of interest.

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